REMARKS

I. Amendments to the Title and Claims

The title of the invention has been amended to clearly define the subject matter of the invention.

Claims 3 and 4 have been amended to clearly define the subject matter of the invention by deleting the terms "managing or preventing a disease associated with undesired angiogenesis, management or prevention, or prophylactically," and by changing "undesired angiogenesis" to "chronic uveitis." Claims 33-39 have been added for doses, dosage formulation and a second active agent. The claims are supported by the originally filed specification and claims. For example, the claims are supported by page 41, line 32; canceled claim 7; page 39, line 6; page 43, lines 8-14; page 49, lines 27-31; page 57, lines 15-20; and page 61, lines 12-19. No new matter has been added.

Claims 1-2, 5-7, 10, 12-24 and 26-32 have been canceled without prejudice. Applicant reserves the right to prosecute the subject matter of any canceled claims in one or more continuation, continuation-in-part, or divisional applications.

Claims 3-4, 8-9, 11, 25, and 33-39 are pending. Applicant respectfully submits that the pending claims are allowable for the following reasons.

II. The Rejection of Claims Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 3-4, 7-9, 11 and 25 are rejected under 35 U.S.C. § 112, first paragraph, on the ground that the specification allegedly does not reasonably provide enablement for "undesired angiogenesis" or "rheumatoid arthritis." (Office Action, pages 3-6). Applicant respectfully traverses this rejection.

It is alleged that claims 3 and 4 recite a very large representation of diseases associated with undesired angiogenesis, and that treating, preventing or managing such diseases is unpredictable, noting that "the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity." (Office Action, pages 4-5). The Examiner claims that it would require undue experimentation to determine the type of angiogenesis disease to be prevented or treated. (Office Action, page 5). Applicant points out that none of

those allegations, alone or in combination, can provide sufficient reason to doubt the fact that the claims are enabled.

Although Applicant strongly disagrees with the Examiner's allegation that the specification is viewed as lacking enablement, solely to expedite the prosecution of the present application, claims 3-4 have been amended to delete the terms "managing or preventing a disease associated with undesired angiogenesis, management or prevention, or prophylactically" and to change "undesired angiogenesis" to "chronic uveitis." Claim 7 reciting "rheumatoid arthritis" has been canceled and the rejection of the claim is moot.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *U.S. v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). The Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. Manual of Patent Examining Procedure (hereafter "MPEP") § 2164.04, (citing *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993)). Furthermore, "[a] specification disclosure...must be taken as being in compliance with the enablement requirement...unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *Id.* (emphasis added).

The amended claims recite, *inter alia*, methods of treating chronic uveitis, by administering a therapeutically effective amount of cyclopropyl-N-{2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-3-oxoisoindoline-4-yl}carboxamide. The specification discloses on page 41, lines 22-32 that chronic uveitis is associated with undesired angiogenesis. The specification also discloses the methods of administration and amounts of the compounds in treating the specified disease. (For example, page 43, lines 4-14 and page 44, line 14 to page 50, line 8 of the specification). Thus, one skilled in the art would have been able to make or use the claimed invention without undue experimentation, based on the methods and amounts of administration set forth in the specification. The determination by a physician as to whether any agent is effective in treating a disease in a given patient is a routine practice and is always performed for every pharmaceutical.

Applicant respectfully submits that the pending claims are enabled, because the specification "contains a teaching of the manner and process of making

and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented." (*See U.S. v. Telectronics, Inc.*, at 785). Applicant respectfully points out that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied. MPEP § 2164.01(b) (citing *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18 (CCPA 1970)) (emphasis added).

The Examiner herself correctly notes that the specification provides an enabling disclosure for methods of treatment of multiple myeloma, a disease associated with undesired angiogenesis. (Office Action, page 3). It is contended, however, that one skilled in the art is unable to predict possible results from the administration of the compound due to unpredictability of the role of angiogenesis. (Office Action, pages 4-5). The specification page 2, lines 8-10 discloses that angiogenesis can be induced through the release of angiogenic cytokines (*e.g.*, TNF-α). Examples 5.1 and 5.3, pages 63-64 of the specification, demonstrate TNF-α inhibitions both *in vitro* and *in vivo* by the recited compounds. Thus, the instant claims are supported by working examples and that there is a recognized correlation between TNF-α inhibition and the treatment of angiogenesis-associated diseases. *See*, also Langer, *Inhibitors of angiogenesis, Biotechnology*, pages 633-4, 1991, submitted herewith, discussing that TNF-α or angiogenesis inhibitors can be used in treating angiogenesis-associated diseases.

As the Examiner is well aware, "[a]n *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a disclosed or claimed method invention." MPEP § 2164.02 (emphasis added). MPEP § 2164.02 also recognizes that "a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence" (quoting *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985)). Where a particular model is recognized as correlating to a specific condition in a given art, the Examiner should accept that correlation, unless the Examiner has evidence that the model does not correlate. (MPEP. § 2164.02; see also *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995)). Thus, the publication and specification support that the correlations between the claimed methods and the *in vitro* and *in vivo*

studies described in the specification. Therefore, a sufficient guidance is provided in the specification so as to allow those of ordinary skill in the art to make and use the claimed invention.

Further, Applicant respectfully submits that "compliance with the enablement requirement does not turn on whether an example is disclosed." MPEP § 2164.02 (citing *Gould v. Quigg*, 822 F.2d 1074, 1078 (Fed. Cir. 1987)). Even in unpredictable arts, a disclosure of every operable species is not required to satisfy enablement. MPEP § 2164.03. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art." MPEP § 2164.08. Thus, one of ordinary skill in the art, armed with the information presented in the specification and publication, has adequate guidance to practice the claimed invention.

Further, Applicant respectfully submits that the selection of a second active agent for use with the compounds recited in the instant claims would require only routine experimentation. Merely routine experimentation is not undue. (See *Wands*, 8 U.S.P.Q.2d at 1404). The specification provides a detailed description of using the second active agent in the combination therapy. (Specification, pages 34-40 and, page 44, line 14 to page 50, line 8). The determination by a physician as to whether any agent is effective in treating a disease in a given patient is a routine practice and is always performed for every pharmaceutical. Thus, Applicant submits that it would require a minimal amount of routine work to practice the claim invention, and one skilled in the art would have been able to make or use the claimed invention without undue experimentation, based on the methods and amounts of administration set forth in the specification.

III. The Written Description Rejection of Claims 3, 4, 8, 9, 11 and 25 Should be Withdrawn

Claims 3-4, 8-9, 11 and 25 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicant respectfully submits that because the present specification does provide an adequate written description, the rejection should be withdrawn.

It is alleged that a laundry list of every possible moiety in a genus does not constitute a written description because it would not reasonably lead to any particular species, and that the applicant has not described diseases associated with

undesired angiogenesis with sufficient clarity. The Examiner states that this rejection can be overcome by including the diseases recited in claim 7 into claims 3-4. (Office Action, pages 6-7).

Although Applicant strongly disagrees with the Examiner's allegation, solely to expedite the prosecution of the present application, claims 3-4 have been amended to change "undesired angiogenesis" to "chronic uveitis" recited in original claim 7. The specification discloses that chronic uveitis is associated with undesired angiogenesis (page 41, line 32). Thus, the recitation of the disease is adequately described in the specification, in such a way that one skilled in the art would recognize that Applicant had possession of the claimed invention at the time the present application was filed. (MPEP § 2161.01).

Therefore, Applicant respectfully requests that the written description rejection be withdrawn.

IV. The Rejection of Claims Under 35 U.S.C. § 102 Should Be Withdrawn

Claims 3-4, 7-8, 11 and 25 are rejected under 35 U.S.C. § 102(e) as anticipated by Man, *et al.* (US 6,667,316 B1, hereinafter referred to "Man"). (Office Action, pages 8-9). Applicant respectfully disagrees.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." (*Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)).

The pending claims recite, *inter alia*, methods of treating chronic uveitis, using cyclopropyl-N-{2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-3-oxoisoindoline-4-yl}carboxamide. An essential element of the pending claims is the use of the compound in treating chronic uveitis. Man does not teach the treatment of chronic uveitis using the recited compound. Thus, Man is missing the essential element of the claimed inventions and cannot be used in the rejection under 35 U.S.C. § 102.

Applicant respectfully requests that the rejection under 35 U.S.C. § 102(e) be withdrawn.

V. The Claimed Invention is Not Obvious

Claims 3-4, 7-9, 11 and 25 are rejected under 35 U.S.C. § 103(a) as obvious over Man in view of Hariri, *et al.* (US 2003/0235909, hereinafter referred to "Hariri") (Office Action, pages 10-12). Applicant respectfully disagrees.

Applicant points out that the present application, Man and Hariri were commonly owned by Celgene Corporation at the time the invention of this application was made. As seen in the cover page of US patent no. 6,667,316, the patent was assigned to Celgene Corporation. Applicant respectfully submits herewith a copy of assignment of Hariri to Celgene Corporation.

As Man and Hariri qualify as prior art only, if at all, as being available as art under 35 U.S.C. § 102(e), the common ownership is sufficient to disqualify the references as a prior art in 35 U.S.C. § 103 rejection. *See, e.g.*, 35 U.S.C. § 103(c) and MPEP § 706.02 (l)(1) and § 706.02 (l)(2). Therefore, neither Man nor Hariri is prior art and for this reason alone the rejection under 35 U.S.C. § 103(a) over the references should be withdrawn.[1]

In view of the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C. § 103(a) be withdrawn.

VI. The Double Patenting Rejection Should Be Withdrawn

Claims 3-4, 7-9, 11 and 15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 3, 7 and 14 of U.S. Patent Application No. 10/515,270. (Office Action, pages 12-13). Since the rejection is provisional, Applicant respectfully requests that the rejection be held in abeyance until the claims are found otherwise allowable.

CONCLUSION

In view of the foregoing, all the rejections of the claims should be withdrawn. Reconsideration, entry of the above amendment and remarks, and allowance of the pending claims are respectfully requested. Should the Examiner not

[1] Applicant reserves the right to present further arguments demonstrating the differences between the claimed invention and Man or Hariri. However, in view of the fact that Man or Hariri is not prior art, this rejection must be withdrawn.

agree that all claims are allowable, a personal or telephonic interview is respectfully requested to discuss any remaining issues and to accelerate the allowance of the above-identified application.

Respectfully submitted,

Date: February 7, 2007

(Reg. No.)

By: Yeah-Sil Moon 52,042

For: Anthony M. Insogna 35,203

JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 326-3939